

# HEMODILUTION: MODELING AND CLINICAL ASPECTS

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**Abstract**-Hemodilution is defined as the dilution of the concentration of red blood cells and plasma constituents by partially substituting the blood with colloids or crystalloids and it is a strategy to avoid exposure of patients to the hazards of homologous blood transfusions. Several mathematical models and computer simulations have been introduced to validate the efficacy of hemodilution; the amount of maximal allowable blood loss and final postoperative hematocrit or hemoglobin has been calculated. The basic prerequisite for preserving tissue oxygenation during hemodilution is adequate oxygen delivery and therefore all determinants of oxygen transport should be monitored. Compensatory mechanisms such as increased cardiac output and stroke volume occur following hemodilution. When debating the use of colloid and crystalloid during fluid replacement, it is imperative to think about all of the components of the Starling equation. In order to better analyze the clinical outcome of hemodilution, more realistic mathematical models should be developed.

**Keywords** - Hemodilution, hematocrit, hemoglobin, oxygen delivery, mathematical models, colloids, crystalloids

## I. INTRODUCTION

Normovolemic hemodilution implies dilution of the normal blood constituents, occurring after injury or blood loss or as a result of plasma replacement or expansion. As a result of acute normovolemic hemodilution (ANH), blood subsequently lost during surgery contains proportionally fewer red blood cells per milliliter, thus minimizing intraoperative loss of autologous erythrocytes and potentially improves tissue perfusion. Preoperative hemodilution was primarily intended to meet the general shortage of homologous (bank) blood during surgery and to avoid its hazards. It is also alternative to the homologous blood due to shortage in blood supply.

Instead of simultaneously exchanging the patient's blood versus a cell-free solution as seen in ANH, some studies used acute preoperative volume expansion without any blood removal and considered this technique as hypervolemic hemodilution (HHD).

Several mathematical and computer models have been developed to more accurately predict the efficacy of hypervolemic and normovolemic hemodilution. To determine the efficacy of each technique maximal allowable blood loss and final postoperative hematocrit or hemoglobin and oxygen transport to tissues should be calculated.

## II. METHODOLOGY

Since the red blood cell (RBC) mass is most suitable to reveal changes in the ratio of main blood constituents, the large-vessel hematocrit (normal 36-45% in females and 42-

50% in males) is used to define the degree of hemodilution. It is, however, important to note that both the hematocrit and the hemoglobin concentration respectively reflect only the concentration of the vehicle transporting oxygen in blood; they do not represent the clinical parameter in hemodilution, which is oxygen content ( $\text{CaO}_2$ ) of arterial blood.

The basic prerequisite for preserving tissue oxygenation during hemodilution is adequate oxygen delivery. The determinants of oxygen delivery are summarized in Figure 1.

Limited or moderate hemodilution denotes a decrease of hematocrit from the normal value to 30%, or slightly lower, whereas a reduction of hematocrit to or 20% or below is termed extreme or severe hemodilution.

To determine the amount of blood that should be removed to reach the desired hematocrit, various formulas and nomograms have been proposed. A simplified formula was presented in 1983 that approximates the logarithmic formula throughout the range of clinical applicability and closely correlates with the observed data:

$$V_L = \text{EBV} \times \frac{H_0 - H_F}{H_{AV}}$$

where  $V_L$  is the allowable blood loss (i.e., the volume of autologous blood withdrawn initially) ; EBV is the estimated blood volume;  $H_0$  is the patient's initial hematocrit (or hemoglobin concentration); and  $H_{AV}$  is the average of the initial and minimal allowable hemoglobin concentrations or hematocrits.

$\text{DO}_2 = \text{Arterial oxygen content} \times \text{Total systemic flow}$

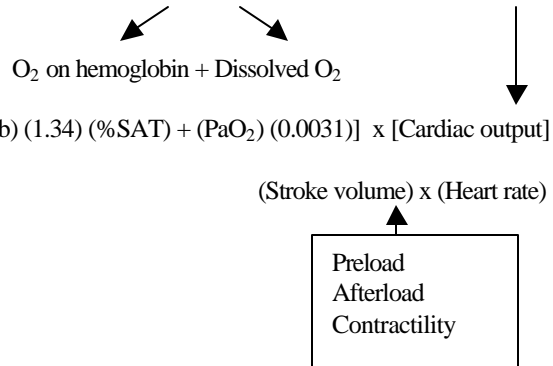


Fig. 1. Systemic oxygen delivery –  $\text{DO}_2$  (ml/min) – is determined by the product of the oxygen content of the blood and total systemic blood flow. The major determinants of components are pictured. Hb = hemoglobin; %SAT=percentage saturation of Hb;  $\text{PaO}_2$  = partial pressure of oxygen in arterial blood; 0.0031 = solubility coefficient for oxygen in plasma [5].

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The final postoperative hematocrit and maximum allowable surgical blood loss with HHD can be calculated as:

$$H_{HHD} = H_0 \times \frac{EBV}{EBV + V_{HHD}}$$

$$V_L = (EBV + V_{HHD}) \times \ln\left(\frac{H_{HHD}}{H_F}\right)$$

Where  $V_{HHD}$  is the volume after HHD;  $H_{HHD}$  is hematocrit after HHD.

Because maintenance of normovolemia is a precondition for safe hemodilution, the acute withdrawal of autologous blood must be simultaneously replaced by a suitable hemodiluent. Ideally, it is achieved by isovolemic exchange transfusion of a plasma substitute with a colloid osmotic pressure (COP) similar to that of plasma. Crystalloids have a short intravascular half-life (20-30 minutes) compared with colloids, and massive infusion of crystalloid solutions carries the risk of acute fluid overload and tissue edema. Thus shortly after induction of hemodilution with crystalloids the patient may become hypovolemic and require additional fluid substitution. A colloid is a fluid containing particles that are large enough to exert an oncotic pressure across the microvascular membrane. In comparison with crystalloids, they have greater intravascular persistence. The duration of intravascular persistence depends on molecular size, shape and ionic charge.

When debating the use of colloid and crystalloid, it is imperative to think about all of the components of the Starling equation:

$$Q = k[(P_{capillary} - P_{interstitial}) - s(\delta_{capillary} - \delta_{interstitial})]$$

Where  $Q$  is fluid movement out of the intravascular space;  $k$  is membrane filtration coefficient;  $P$  is hydrostatic pressures;  $\delta$  is colloid osmotic pressures;  $s$  is membrane reflection coefficient (Permeability to proteins)

### III. RESULTS

The efficacy of HHD, ANH and no preoperative hemodilution has been compared by a number of mathematical models. It has been shown that compared to no hemodilution, HHD and ANH always give higher final hematocrit values and provide red blood cell savings, which can be considered clinically relevant. HHD has always revealed lowest maximal allowable blood losses, thus making HHD the technique that requires homologous blood transfusions first (Fig. 2).

It has been identified that two requirements have to be met to sustain systemic oxygen capacity during

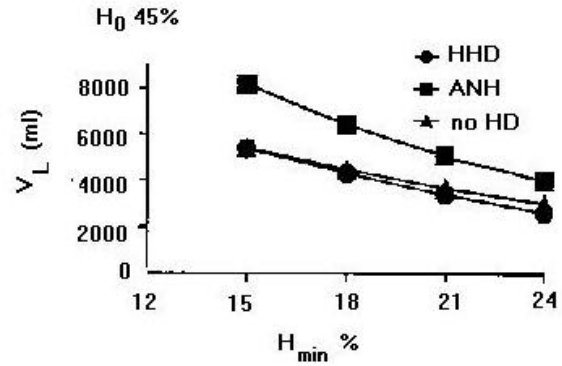


Fig. 2. The relationship between minimal acceptable hematocrit ( $H_{min}$ ) and maximal allowable surgical blood loss for HHD, ANH and no hemodilution (HD) with initial hematocrit of 45%, modified from [1].

hemodilution, at normal values; these are a) maintenance of normovolemia and b) normal cardiovascular function (Fig. 3). So long as normovolemia is preserved, the hematocrit level does not fall down below 25%, and the patient is in the resting state, stroke volume and cardiac output increase and the heart rate remains constant. The increase of cardiac output amounts to 30% to 50% at a hematocrit of 30% even in the presence of anesthesia.

In an anesthetized and hemodiluted patient a rise in heart rate during or shortly after the dilution procedure indicates either inadequate cardiac output or hypovolemia due to loss of the plasma substitute from the intravascular space.

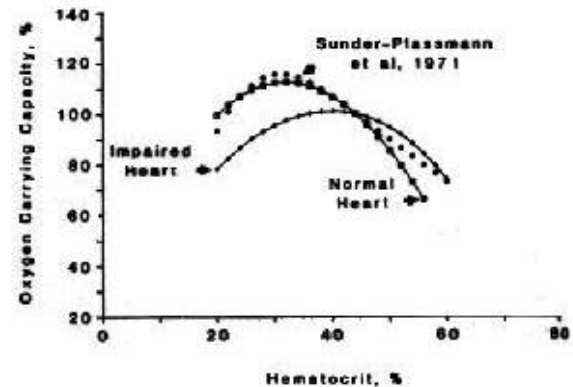


Fig.3. Systemic oxygen carrying capacity in dependence upon the hematocrit. The figure contains experimental data obtained from healthy dogs undergoing isovolemic hemodilution, together with data obtained from model analyses by Mirhashemi. Hemodilution in presence of impaired heart function is associated with a substantial reduction of systemic oxygen transport capacity when hematocrit falls below 40 % [2].

#### IV. DISCUSSION

Preoperative hemodilution to avoid or decrease the need for homologous blood transfusions has become increasingly popular over the past 20 years. Hemodilution minimizes the hazardous effects associated with transfusion of homologous blood, namely transmission of viral diseases, immunosuppression, and infectious complications, it is feasible and relatively cost-effective.

It is possible to find models of hemodilutions as applied to medical and educational simulators. The impact of hemodilution on total blood volume, plasma volume and the amount of hematocrit and/or hemoglobin concentration, oxygen delivery to tissues has been incorporated in the "hematology model" which is a part of Human Patient Simulator (HPS). HPS is a full-scale patient mannequin with cardiovascular and pulmonary computer driven models and its simulator environment is used to teach and practice the management of preoperative medical events and emergencies.

Most of the publications on preoperative hemodilution and its mathematical validation have many severe assumptions and limitations. Therefore, more realistic and more exactly calculated mathematical models based on clinical practice should be developed.

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